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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/867,847	CHALIFOUR ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,12-17 and 21-39* is/are pending in the application.

4a) Of the above claim(s) *21-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 12-17* is/are rejected.

7)☒ Claim(s) *3-7 and 12-16* is/are objected to.

8)☒ Claim(s) *1-8,12-17 and 21-39* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 October 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6-10-03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

1. The IDS of 6-10-03 has been entered into the record and has been fully considered as indicated on the attached PTO-149.

2. The amendment filed 10-27-03 has been entered into the record and has been fully considered. Claims 1-8, 12-17 and 21-39 are pending.

3. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

4. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn by the Examiner.

Rejections Maintained

Drawings

5. The drawings are again objected to because the legends, i.e., "Figure X" is illegible. The proposed drawing correction of 10-27-03 does not incorporate changes to the figure legends. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Election/Restriction

6. Applicant's election with traverse of Group I, claims 1-8 and 12-17 to the extent of methods of treating or preventing by administration with a peptide of SEQ ID NO:15, in Paper No. 14(12-31-02) is acknowledged.

Applicant's arguments of 10-27-03 with respect to the Restriction requirement are noted. In particular Applicants request clarification of the statement that examination

has been carried out to the extent of the elected SEQ ID NO in that they believe the Examiner has read such as a limitation of all claims. In addition, Applicants argue that the invention provides unity in that all peptide members are used as vaccine antigens and are related as immunogenic fragments of beta-amyloid. Applicants argue that the guidance for restriction amongst Markush groups/Unity of invention does not require that the members share all uses and all structural features. Applicants argue that there is no substantial burden for search and examination in that the number of members are few, related and not burdensome for examination of the full scope of the generic claim.

Applicant's arguments submitted 10-27-03 have been fully considered but are not persuasive. The Examiner has examined the noted generic claims as indicated by their rejection as set forth. It is noted that the prior art of record is directed to Applicants elected SEQ ID NO. The generic claims have been examined and considered by the Examiner but search and examination of all peptide members is not required in that the peptides as deemed to be patentably distinct and prior art to the elected member has been established. The Examiner is not required to cite all relevant art to the generic claims, but only that deemed best for prosecution. The art cited is deemed best in that it is directed to the elected SEQ ID NO. The Examiner does not view the sequence as a limitation of the generic claim. Nevertheless, the art of record is pertinent to the generic claims and to particular sub-generic claims as indicated. In contrast to Applicant's analysis, the members of the generic claims are extensive, not few and the search and examination of all the peptide sequences within a single application is deemed burdensome to the Office and to the Examiner. It is further noted with respect to Unity

of invention/Markush language that the generic claims are not structurally related to beta-amyloid as asserted by Applicant's. For example, there is no limitation as to peptide structure within generic claim 1. In addition, the Office views the recited peptide members as patentably distinct as previously set forth, and restriction for examination purposes is therefore deemed proper. The generic claims are neither deemed free of the prior art nor allowable for the reasons of record.

7. Claims 21-39 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14. Applicant's also present further arguments as to the restriction requirement as presented in the amendment of 10-27-03, addressed herein.

8. This application contains claims 21-39 drawn to an invention nonelected with traverse in Paper No. 14. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Double Patenting

9. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and In re Goodman, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory

double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-8 and 12-17 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 46-56, 58-64, and 66-109 of copending Application No. 09/724,842. Although the conflicting claims are not identical, they are not patentably distinct from each other because the comprised peptides overlap with instantly elected SEQ ID NO:15. In particular it is noted that the claims similarly recite methods of preventing and treating amyloid related diseases including via administration with all-D peptides. It is noted that the peptides either share the common structure of SEQ ID NO:15 or are identical. In particular SEQ ID NO's 13 and 21 share the same structure and length as SEQ ID NO:15. Moreover, the claims similarly recite the administration of the same peptides with the same alternative N'terminal and C'terminal modifications as recited for example in instant claims 4-8 and 12-17. The administration is of the same compounds to the same individuals for the same purpose and thus inherently share all functional components as recited such as inducing an immune response, eliciting the production of antibodies, interacting with an amyloid protein and thereby preventing or reducing neurodegeneration, cellular toxicity and amyloid fibril formation. Thus, the co-pending claims render the instant claims obvious to the skilled artisan.

This is a provisional obviousness-type double patenting rejection because the

conflicting claims have not in fact been patented.

Applicants argue in the response of 10-27-03 that all other issues being moot, that the first application should be allowed to issue.

Applicant's arguments filed 10-27-03 have been fully considered but are not persuasive because the instant application is rejected as set forth herein. Thus, all other issues are not moot and the provisional double patenting rejection is properly maintained for the reasons of record.

Claim Objections

11. Claims 3-7 and 12-16 stand objected to as reciting an improper Markush Group. M.P.E.P. 803.02 states that:

> Since the decisions in In re Weber, 198 USPQ 328 (CCPA 1978); and In re Haas, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention, In re Harnish , 631 F.2d 716, 206 USPQ 300 (CCPA 1980); Ex Parte Hozumi , 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility.

In instant case the encompassed peptides differ substantially in structure and are capable of different use, with different modes of operation, different function and different effects. Therefore the peptides lack unity of invention.

Applicants argue in the amendment of 10-27-03 that the generic claims should not have been objected to in that they are generic and are not drawn to Markush groups. In particular Applicants argue that only claims 3-5, 8, 12, 14 and 17 are directed to Markush groups of amyloid fibrils or proteins. Claims 4, 5, 12 and 14 are argued to be directed to substituents that are commonly examined together.

Applicants arguments filed 10-27-03 have been fully considered but are

persuasive only in part. Another way of stating the previous objection is that the claims are objected to for being drawn to non-elected subject matter. To the extent that claims 1 and 2 are truly generic to the peptides encompassed, Applicants arguments are deemed persuasive. There would be nothing to cancel from the claims as non-elected should that subject matter be found allowable. However, the generic recitations are rejected for the reasons of record and are not deemed to be allowable. Objection of claims 8 and 17 are withdrawn in that the Examiner notes their recitation of the elected subject matter alone and similarly there would be nothing to cancel from the claims. However, claims 8 and 17 are rejected as noted herein. Objection to claims 3-7 and 12-16 stand in that the claims recite multiple members that are not all drawn specifically to the elected SEQ ID NO: and substituents. Thus, the claims are drawn at least in part, to non-elected subject matter. The claims are further sub-generic to the invention. Were the subject matter elected found to be allowable, particular claims may be objected to as being drawn to non-elected subject matter, i.e., sub-generic groups not allowable or specific members not allowable. Alternatively at that time the Examiner may consider re-grouping or allowance of particular sub-generic or member recitations. However, at this time, the claims are properly rejected and thus Unity of Invention is lacking, and the claims may be objected to as reciting improper Markush groups and/or as being drawn to non-elected subject matter. Upon the determination of allowable subject matter, regrouping may be considered by the Examiner. See also the above comments with respect to maintaining the restriction requirement.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-8 and 12-17 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling as supported in the literature for reducing beta-amyloid plaque burden in cortical regions of PDAPP transgenic mice via administration of AN1792 (human Aβ1-42), rodent Aβ1-42 and Aβ1-5 conjugated to sheep anti-mouse IgG as exemplified and disclosed for example in Schenk et al., WO99/27944 published 10 June 1999, does not reasonably provide enablement for preventing or treating amyloid related disease, particularly in a human patient or for preventing or treating such diseases with the breadth of peptides claimed. In particular the breadth of the peptides as claimed encompasses all peptides capable of providing for the claimed functional effects that are in 50% portion, D-amino acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to make and use the invention commensurate in scope with these claims.

The disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

The claims are drawn to a method for treatment and prevention of amyloid

related diseases via administration of D-amino acid peptides. The specification fails to exemplify any such treatment but references Schenk et al., 1999 Nature 400:173-177 as a basis for such prevention or treatment. Schenk teaches that the administration of particular polypeptides is able to reduce beta-amyloid levels within the brains of mice that are transgenic for PDAPP. These mice exhibit Alzheimer's type over production and build up of beta-amyloid within the brain. However, as recognized in the art, these mice do not exhibit Alzheimer's disease as in humans or plaque morphology and components which are the same as in humans, Alzheimer's disease, Down's Syndrome or other amyloidogenic diseases, see in particular Schenk et al., Nature, 400:173-77, 1999 (IDS), Games et al., Nature 373(6514):523-7, 1995 (IDS) and Chen et al., Progress in Br. Res., 117:327-34, 1998. Thus, the model system used is not recognized as providing for teachings that are predictive of the results that would be expected for the full scope of the claims, including for any amyloid related disease or for such diseases in humans. For example, the art recognizes that such in vivo models are not readily correlated to the human in vivo case. In particular, the art teaches a lack of correlation of beneficial effects shown in the mouse model system in humans, see in particular Munch et al., J. Neural Transmission, 2002 July, 109(7-8):1081-87. Specifically, treatments effective in mice were shown to evoke neurotoxicity when practiced in humans. Thus, for the aforementioned reasons treatment of humans does not appear to be commensurate in scope with the claims.

Moreover, the model system does not fairly teach that the treatment is effective to prevent the onset of disease. Alternatively, the teachings exhibit a reduction of

pathogenic characteristics in Alzheimer-like pathology, but fail to teach the prevention of plaque development in animals. As evidence, the Examiner notes that all PDAPP mice exhibited plaques regardless of treatment regime. Even the most effective treatments were only effective to reduce the plaque burden in animals, not prevent it.

The method is based upon findings that show particular strategies of targeting plaque removal via antigen administration. Evidence that such therapy can be effective in the removal of amyloid plaque burden is exhibited by Lemere et al., Society for Neuroscience Abstracts, vol. 25, part I, Abstract 519.6, 29th Annual Meeting 10/23-10/28, 1999 using antigen Aβ1-40 and Schenk, Nature, 400:173-177, 1999 (IDS) using antigen Aβ1-42. Similarly Nordstett and Kiessling as set forth below teach treatment of Alzheimer's disease and amyloid plaque deposits via administration of the KVLFF sequence. However, what these references do not teach is the relative ability of other alternative peptides to achieve such effects.

The skilled artisan readily recognizes that protein chemistry is an unpredictable area of biotechnology. Proteins with deletion, insertion or substitution/replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. For example, Jobling et al, Mol. Microbiol., 1991, 5(7):1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which produce proteins that differ in native conformation, immunological recognition, binding and toxicity. The skilled artisan further recognizes that immunological responses may depend upon the structural characteristics

(conformation) of the particular protein (amino acid sequence) targeted. Thus, both biological function and immunological recognition are unpredictable properties which must be experimentally determined. Further it is noted, that for particularly small peptides, conjugation appears to be required for promoting an effective immune response.

These concepts are exemplified within Schenk WO99/27944. For example, the specification discloses experimentation using a group of human Aβ peptide sequences consisting peptides of 1-5, 1-12, 13-28, and 33-42 conjugated to sheep anti-mouse IgG, see in particular pp. 62, lines 25-32. Yet only the conjugated fragment of Aβ1-5 was effective to reduce plaque burden in PDAPP mice, and only within the cortex, see in particular pp. 64, lines 30-31. Thus, the specification exemplifies the unpredictable nature of providing prevention or treatment with variable but even highly related peptides. Thus, the Schenk publication evidences the unpredictability and variability in the effectiveness of peptide immunogen constructs in effecting amyloid plaque removal or treatment of amyloid related diseases. Thus, the specification does not enable the broad scope of the claims which encompass a multitude of analogs or equivalents because the specification does not teach which residues can or should be modified such that the polypeptides retain sufficient structural similarity to evoke immune responses that would provide for treatment or preventative effects. The specification provides essentially no guidance as to which of the nearly infinite possible choices is likely to be successful and the skilled artisan would not expect functional conservation among homologous or variable sequences. The artisan cannot predict the protective

epitope structures without further undue experimentation.

Finally, the claims recite the use of an antigenic all-D peptide via it's functional characteristics and not by it's particular amino acid structure. The functions to be provided include a sufficient response to produce antibodies, induce an immune response, prevent or reduce amyloid-induced neurodegeneration or amyloid fibril formation, interact with an amyloid protein, and the ability to prevent or reduce amyloid-induced cellular toxicity. Yet the specification does not exemplify which peptides are particularly able to produce such effects. Thus, the claims are akin to a single means claim, i.e., where a means recitation does not appear in combination with another recited element of means and is subject to an undue breadth rejection under 35 USC 112, first paragraph because the specification at most would only disclose those means known to the inventor at the time of the invention, see in particular MPEP 2164.08(a). While the artisan may recognize particular peptides that have been shown to be effective, such is not commensurate with the scope of all peptide sequences that are as yet not identified but which are capable of producing the claimed effects. The specification fails to provide a suitable methodology for determining or predicting the success of peptide sequences for producing the requisite effects and thus the enablement provided by the specification is not commensurate with the scope of the claims.

Therefore, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable

correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

In view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue experimentation to make and use the claimed invention.

Applicants argue in the amendment of 10-27-03 that the animal models of amyloid related disease in use at the time of the invention were known to the artisan and used in studies for the identification and characterization of potential treatments in humans and that just because not every feature of disease is mimicked does not mean the models do not have predictive value. Applicants point to Chishti, Janus and Morgan for such assertion. Applicants further argue that Hock and Cirrito evidence that such treatments may be effective and point to the Gervais declaration as providing evidence that D peptides may be effective in decreasing amyloid burden. Applicants argue that Skolnick and Jobling do not evidence that mutations necessarily decrease immunoloigcal recognition. Applicant's further argue that the art recognizes the ability of screening techniques for various peptides, antibodies or compounds directed at decreasing amyloid fibrils, i.e., antifibrillogenic activity as assessed in vitro, to be reasonably predictive in vivo and thus would not require undue experimentation. Thus,

applicants conclude that sufficient guidance is provided within the specification to identify and characterize the candidate peptides without undue experimentation.

Applicant's arguments filed 10-27-03 have been fully considered but are not persuasive. In particular, Applicant's referral to particular references is improper as such references have not been formally made of record on any PTO-1449. While the Chishti, Janus, Morgan, Hock and Cirrito references were transmitted they have not been formally considered by the Examiner but have been placed in the file. Nevertheless, while the Chishti, Janus, Morgan, Hock and Cirrito references appear by Applicants assertion to provide a basis for such experimentation, the references fail to establish the predictability of any particular peptide administration in providing for prevention or treatment of amyloid-related diseases as claimed in subjects at the time of the invention. Nor does it appear that instant peptides have been subjected to such exemplary testing with respect to treatment or prevention. As to the Gervais declaration, such declaration was not apparently transmitted or received by the Office and thus the declaration has not been entered into the record or considered by the Examiner. Nevertheless, the Gervais declaration by Applicant's assertion speaks only to effects in stimulating an immune response (as apparently measured by antibody titers) to particular peptides tested which are apparently all D, not 50% D as claimed and not of a sufficient number or breadth to support instant claims with respect to prevention or treatment of amyloid related diseases in patients. In contrast to Applicant's analysis, the cited references and declaration speak to the unpredictable nature of such peptides in providing for treatment or prevention as claimed as the

testing is not commensurate. The exemplifications therein fail to correlate in scope with instant claims. The specification provides no exemplary peptides tested in the aforementioned assays whereby the artisan would recognize correlation to provide for prevention or treatment of amyloid-related diseases in vivo. Thus, for the aforementioned reasons, the experimentation required to make and use the claimed invention is undue.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

15. Claims 1-8 and 12-17 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nordstedt et al., WO97/21728 published 19 June 1997 and under 35 U.S.C. 102(e) as being anticipated by Nordstedt et al., US Patent No. 6,331,440 filed June 10, 1998. These rejections are set forth in conjunction as the references are cumulative. However, as noted, the references apply under different statutes.

Nordstedt et al., teach peptide binding sequences of beta amyloid useful as

medicaments and as tools for identification of substances to be used in the treatment or prevention of amyloidosis, see in particular Abstract and Introduction. In particular peptides comprising the peptide KLVFF are disclosed as useful for treatment of Alzheimer's disease, see in particular Summary of the invention and Detailed description of the invention. As noted therein, all of the amino acids may be either of D- or L-isomers. In addition, as represented by R1 and R2 in the formula R1-A'-Y'-Leu-X'-Z'-B-R2, the N-terminal substituents may be of H (hydrogen) or -CO-R3 bonded at the amino group of A'. Also, the C-terminal substituents may be of hydrogen OR4 or NR5R6 bonded to the carboxyl group of the carboxy terminal B' as set forth in the Detailed description of the invention. As substituted at the N' and C'terminus the substituents of Nordstedt are the same as claimed, i.e., hydrogen (hydroxy), alkyl (alkoxy), cycloalkyl, aryl (aryloxy), or (substituted amino), (as claimed). The substituents constitute acid functional groups and pharmaceutically acceptable salt or ester forms suitable for administration, see in particular Detailed description of the invention for the treatment and prevention of fibril formation of human amyloid protein as in Alzheimer's disease. The peptides are administered to the same patient groups in the same form and for the same purpose as claimed. Such peptides are extensively recognized as capable of eliciting an immune response, see in particular Schenk et al., of record. Thus, all functional limitations are necessarily provided absent convincing factual evidence to the contrary. Therefore, the reference teachings anticipate the claimed invention.

Applicants argue in the amendment of 10-27-03 that the Norstedt reference fails

to teach the induction of an immune response as required by the claims, that the reference teaches the use of such peptides to inhibit amyloid fiber formation by competitive inhibition and that Schenk does not teach that the peptides are capable of eliciting an immune response as the peptides are not D.

Applicants arguments filed 10-27-03 have been fully considered but are not persuasive. In particular, it is noted that the administration is the same as set forth. The Norstedt peptides are all or partially L or D as disclosed. It is Applicant's burden to show unobvious distinction to the inherent property of the peptides and their immunogenicity. Applicant's comments with respect to the references' teachings of the ability to inhibit amyloid fibril formation correlates with Applicants arguments within the 112, first paragraph rejection that such peptides would be recognized by the artisan as suitable for treatment and/or prevention of amyloid-related diseases. In accordance with In re Best, see MPEP 2112.

A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC. Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same

rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C.102/103 rejection is appropriate for these types of claims as well as for composition claims.

Comparison by the office is not required. As to applicants apparent referral that the peptides are not D, the claims do not require that the peptides be of all D form, but only of at least 50% D form. Nevertheless the Norstedt peptides are of the required D form. In addition, the record is clear that the artisan as well as Applicants view the D peptides as immunogenic. Nevertheless, as noted herein, the artisan well recognizes that D amino acids are immunogenic, see in particular IDS reference WO 94/05311 Deakin Research Limited, 03/17/1994 cited by Applicant and previously of record which teaches the immunogenicity of D-amino acid peptides within the host. Thus, the reference teachings anticipate the claimed invention and proof of unobvious difference shifts to Applicants.

16. Claims 1-8 and 12-17 stand rejected under 35 U.S.C. 102(e) as being anticipated by Kiessling et al., US Patent No. 6,022,859 filed February 8, 2000.

Kiessling et al., teach peptide inhibitors of beta-amyloid toxicity, see in particular Abstract. The peptide comprises the recognition element sequence KLVFF. The peptide disrupts beta-amyloid aggregation and interferes with its toxicity, thereby providing a therapeutic reagent for treating Alzheimer disease patients, see in particular Brief Summary of the Invention. The peptide maybe of D-amino acids, substituted or unsubstituted including via alkyl, alkoxy, hydroxy and carboxy, see in particular column 4 and 14. The preparation may be for pharmaceutical use and may be accordingly

modified via buffering agents including for pharmaceutically acceptable salt or ester forms, see in particular columns 5-6. The peptides are administered to the same patient groups in the same form, for the same purpose as claimed. Such peptides are extensively recognized as capable of eliciting an immune response, see in particular Schenk et al., of record. Thus, all functional limitations are necessarily provided absent convincing factual evidence to the contrary. Therefore, the reference teachings anticipate the claimed invention.

Applicants argue in the amendment of 10-27-03 that the Kiessling reference fails to teach the induction of an immune response as required by the claims, that the reference teaches the use of such peptides to inhibit amyloid fibril formation by competitive inhibition and that Schenk does not teach that the peptides are capable of eliciting an immune response as the peptides are not D.

Applicants arguments filed 10-27-03 have been fully considered but are not persuasive. In particular, it is noted that the administration is the same as set forth. The Kiessling peptides are partially L or D as claimed and the substituents are the same. It is Applicant's burden to show unobvious distinction to the inherent property of the peptides and their immunogenicity. Applicant's comments with respect to the references' teachings of the ability to inhibit amyloid fibril formation correlates with Applicants arguments within the 112, first paragraph rejection that such peptides would be recognized by the artisan as suitable for treatment and/or prevention of amyloid-related diseases. In accordance with In re Best, see MPEP 2112.

A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR

ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC. Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C.102/103 rejection is appropriate for these types of claims as well as for composition claims.

Comparison by the office is not required. As to applicants apparent referral that the Schenk peptides are not D, the claims do not require that the peptides be of all D form, but only of at least 50% D form. However, the record is clear that both the artisan as well as Applicant's view the D peptides as immunogenic. Nevertheless, as noted herein, the artisan well recognizes that D amino acids are immunogenic, see in particular IDS reference WO 94/05311 Deakin Research Limited, 03/17/1994 cited by Applicant and previously of record which teaches the immunogenicity of D-amino acid peptides within the host. Thus, the reference teachings anticipate the claimed invention and proof of differences shifts to Applicants.

Status of Claims

17. No claims are allowed.

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
December 30, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600